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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/578,669	05/25/2000	Kenneth H. Grabstein	2831-E	7760

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IMMUNEX CORPORATION
LAW DEPARTMENT
51 UNIVERSITY STREET
SEATTLE, WA 98101

EXAMINER
NAVARRO, ALBERT MARK

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/578,669	Grabstein et al
Examiner	**Art Unit**
Mark Navarro	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *26-63* is/are pending in the application.

4a) Of the above, claim(s) *30-34, 39, 42, 45, and 47-63* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *26-29, 35-38, 40, 41, 43, 44, and 46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 26-29, 35-38, 40-41, 43-44 and 46 in Paper No. 10 (received September 12, 2002) is acknowledged. The traversal is on the ground(s) that Groups I and II are related as conjugated forms of IL-15 and IL-15 muteins, and that the Examiner has failed to acknowledge the presence of a linking claim (claim 26), and that all groups of the invention are closely related and, therefore, would require common areas of search and consideration, and that MPEP 803.04 is directed to nucleotide sequences, while the instant application is directed to proteins. This is not found persuasive because Groups I and II are each directed to biological molecules with a distinct primary, secondary, and tertiary structure. Each of these structures necessitate a separate search and consideration of the prior art. As set forth in MPEP 803.04 proteins which are structurally distinct from each other are unrelated to one another. In the instant application, a single amino acid substitution, insertion or deletion, generates an unrelated molecule which is properly restricted from the wild type molecule. It is noted that Applicant's have a linking claim in claim 26. However, a linking claim must recite equivalent species, as set forth above the generation of a distinct primary, secondary, and tertiary protein structure generates a restrictable compound even when present in a linking claim. (e.g. selected from the group consisting of an antibody, bowling ball, bicycle and golf ball). Finally, the

separate classification of the groups is one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is adhered to.

Furthermore, Applicant's newly submitted claims 56-63 are also drawn to method claims that have been restricted from the elected antagonist group for the same reasons set forth in Paper Number 7, mailed February 1, 2002. Accordingly, these claims are also withdrawn from further consideration as being drawn to a non-elected invention.

Accordingly, claims 26-63 are pending in the instant application, of which claims 30-34, 39, 42, 45, and 47-63 are withdrawn from further consideration as being drawn to a non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. Claims 26-27, 35-38, 40-41, 43 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 26-27, 35-38, 40-41, 43 and 46 recite an antagonist of IL-15 activity comprising IL-15 conjugated with a chemical group that sterically interferes with the ability of IL-15 to transduce a signal through the IL-15 receptor complex.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the recitation of antagonist of IL-15 alone is insufficient to describe the genus. Thus, Applicant's have not described a structure which is shared by the antagonist which would adequately describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 26-29, 35-38, 4041, 43-44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giri *et al* and Grabstein *et al* in view of Ferrara et al and Hakimi et al.

The claims are directed to an antagonist of interleukin 15 activity comprising IL-15 conjugated with a chemical group that sterically interferes with the ability of IL-15 to transduce a signal through the IL-15 receptor complex.

Giri et al (The EMBO Journal Vol. 13 (12), pp 2822-2830, 1994) teach of the cytokine IL-15 having shared bioactivities with IL-2. Giri *et al* further teach that analysis of IL-15 interaction with subunits of the IL-2 receptor revealed that the α subunit was not involved in IL-15 binding. Giri *et al* further set forth that both the β and γ chains are required for IL-15 binding and signaling. (See abstract).

Grabstein *et al* (Science Vol. 264, pp 965-968, May 13, 1994) teach that monoclonal antibodies to the β-chain of the IL-2 receptor inhibited the biological activity of IL-15. (See abstract).

Neither Giri et al nor Grabstein et al teach of an antagonist of IL-15 comprising IL-15 conjugated with a chemical group that sterically interferes with the ability of IL-15 to transduce a signal through the IL-15 receptor complex.

Ferrara *et al* (Journal of Immunology Vol. 137 (6), pp 1874-1877, Sept 15, 1986) teach that the severity of GVHD was reduced by both clinical and histologic parameters when transplant

recipients received injections of a monoclonal antibody directed against the interleukin 2 receptor. (See abstract)

Hakimi et al (U.S. Patent Number 5,539,063) teach that when proteins are conjugated with PEG it results in a substantial loss of protein binding to its receptor. (See column 17).

Given that 1) Giri et al and Grabstein et al have taught of the interleukin 15 molecule and its bioligically shared bioactivities with IL-2, and that Ferrara et al have taught of reducing the severity of GVHD by inhibiting the activity of IL-2, and that Hakimi et al has taught that proteins conjugated to PEG result in a substantial loss of protein activity, it would have been prima facie obvious to have taken the IL-15 as taught by Giri et al or Grabstein et al and to have conjugated the IL-15 to PEG as taught by Hakimi et al to create an antagonist of IL-15 activity. One of skill in the art would have been motivated to create such an antagonist in view of the teaching by Ferrara et al that GVHD severity was reduced by inhibiting the activity of IL-2 and the teaching by Giri et al that IL-15 has shared bioactivities with IL-2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached

on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

November 14, 2002